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| EXAMINER | |
|---|---|
| GROSS, CHRISTOPHER M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | |

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/798,799 | MEHTA ET AL. | |
| | Examiner | Art Unit | |
| | Christopher M. Gross | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *31 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *6,8,10,13,16,18,19,28,32-35 and 45-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7, 9, 11-12, 14-15, 17, 20-27, 29-31, 36-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/3/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Responsive to communications entered 10/31/2006. Claims 1-50 are pending. Claims 6, 8, 10, 13,16, 18-19, 28, 32-35, 45-50 are withdrawn. Claims 1-5, 7, 9, 11-12, 14-15, 17, 20-27, 29-31, 36-44 are examined herein.

### *Election/Restrictions*

Applicant's election of group I (claims 1-45) in the reply filed on 10/31/2006 is acknowledged. Because applicant did not distinctly and specifically point out any supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election of the species: laser capture microdissection (From claims 3-6); reversed phase protein microarrray analysis (From claims 10-13); a normal cell (From claims 14-16); same subject (From claims 17-19); abnormal growth (From claim 21); post-translational modification (From claims 22-23); EGFr phosphorylation and non-voltage gated calcium ion channels (From claim 26); specific Cox-2 inhibitor and carboxyamidotriazole (CAI) (From claims 30-35); a growth factor pathway (From claim 38), encompassed in claims 1-5, 7,9-15,17,20-27,29,30,31 and 36-44 in the reply filed on 10/31/2006 is acknowledged.

Even though Applicant states that claims 10 and 13 read on the elected species mentioned above, however the Examiner respectfully disagrees. Claims 10 and 13 are not drawn to *reverse phase* protein microarray analysis and stand withdrawn from further consideration.

Claims 6,8,16,18-19,28,32-35,45-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species or invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/31/2006.

***Priority***

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) is acknowledged. This application claims benefit of provisional application 60/453,629 03/10/2003.

***Information Disclosure Statement***

The information disclosure statement filed 9/3/2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible complete copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein regarding citations 5,8, 11-12, 19-22, 27,29-32,34-37,39,43,44,47,48,50,53,56,60,63, 67,70,76,78, 79,81,83,86,88, 93-95,97,101,104-105, 109,120, 128, 121, 123, 126 and 127 has not been considered.

The information disclosure statement entered 9/3/2004 is objected to because relevant pages, and date and place of publication are missing from some of the non-patent documents [See MPEP 609.01, (B)(1)(e)(v)]. The Examiner has **not** initialed citations 17-18, 64, 122 because of the missing information.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5,7,9,11-12, 14-15, 17, 20-27, 29-31, 36-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites vague and indefinite language in a "deranged cell signaling pathway" in the second line. To one of skill in the art, it is not clear what makes a pathway deranged and the specification does not provide a clear definition. Thus, as currently written, the metes and bounds of the claims are unascertainable. Therefore, claim 1 and all dependent claims are rejected under 35 USC 112, second paragraph.

Claim 1 recites vague and indefinite language in the past tense use of "the therapeutic agents are selected to target two or more different members of a protein signaling pathway or network" It is not clear whether the selection represents a method step or whether if the therapeutic agents possess the desired targeting property *a priori*. Thus, as currently written, the metes and bounds of the claims are unascertainable.

Claim 3 recites the limitation "the subject" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 24 recites vague and indefinite language in a "prior success" in the second line. To one of skill in the art, it is not clear what constitutes success and the specification does not provide a clear definition. Thus, as currently written, the metes and bounds of the claim is unascertainable.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2,7,14-15,20-23,36-39,41-42 are rejected under 35 U.S.C. 102(b) as being anticipated by **Bishop et al** (US Patent 6316462).

The claimed invention is drawn to a method for selecting a combination of therapeutic agents for treatment of a disease caused by a deranged cell signaling pathway or cell signaling pathway network that leads to an aberrant cellular response, comprising:

(i) measuring activity states for a plurality of different signaling proteins extracted from a diseased cell, where the signaling proteins are members of one or more signaling pathways or networks;

(ii) determining whether the activity states measured for the plurality of signaling proteins extracted from the diseased cell are different than activity states measured for corresponding signaling proteins from a reference cell to detect differences between the activity states of individual signaling proteins from the diseased cell and the activity states of the corresponding individual signaling proteins from the reference cell; and

(iii) selecting a combination of at least two different therapeutic agents, wherein the therapeutic agents are selected to target two or more different members of a protein signaling pathway or network comprising an individual signaling protein for which a

difference in activity state was detected between the diseased cell and the reference cell, wherein the agents reduce the difference in the activity state that was detected. Claims 2,7,14-15,20-23,36-39,41-42 represent variations thereof.

**Bishop et al** teach, throughout the document, and especially the abstract and figure 1 a method for treating cancer comprising a farnesyl transferase inhibitor (e.g. SCH 66336) and additional Ras signaling pathway inhibitors (e.g. PD 98059 or U0126).

Bishop et al teach in columns 1-2 cancer cells expressing constitutively active, or else overexpress, Ras exhibit abnormal growth and further said Ras pathway inhibitors are either cytostatic or cytotoxic (induce apoptosis) toward the cells exhibiting abnormal growth.

Bishop et al teach in figure 6, measurement ERK 1 and 2 phosphorylation states in Ras transformed (diseased) cells to determine the effectiveness said Ras pathway inhibitors which reads on claim 1 part (i).

Bishop et al teach in figure 5 the Ras transformed cells are more prone to undergo apoptosis in the presence of SCH 66336 plus PD 09859, as compared to untransformed (normal) cells. Cells which undergo apoptosis would *inherently* have a different activity state than that those that do not, thus reading on claim 1 part (ii).

The selection of SCH 66336 plus PD 09859 per Bishop et al reads on claim 1 part (iii).

The untransformed cells of Bishop are taken as the normal cell (elected species) set forth in claim 14 and 15.

Bishop et al teach in column 2 line 48, the combination of Ras pathway inhibitors act in a synergistic manner, reading on claim 2.

The Ras transformed cells of Bishop et al are taken as the diseased cells set forth in claim 7.

Bishop et al teach in claim 53, administration of Ras pathway inhibitors to a patient, reading on the subject of claim 20.

The Ras transformed cells of Bishop et al are taken as exhibiting abnormal growth (elected species) as set forth in claim 21.

The measurement ERK 1 and 2 phosphorylation states per Bishop et al is taken as a post-translational modification (elected species) as set forth in claims 22 and 23.

Bishop teach in column 2 the methods are useful against breast and colorectal cancers, reading on claims 36-37.

Bishop teach in figure 1, the Ras pathway is a growth-factor pathway (elected species) as set forth in claim 38.

The gel in figure 6 of Bishop compares the total amount of ERK 1 and 2 versus the amount of phosphorlyated protein, reading on claim 39.

The increase in phosphorylated ERK shown in Figure 6 of Bishop et al, which is inhibited with PD 098059 and/or SCH 66336 reads on claims 41-42.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,2,7,14-15,20-23,36-39,41-42 and 3-5,9 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Bishop et al** (US Patent 6,316,462) in view of **Bonner et al** (US Patent 6,251,516).

**Bishop et al** is relied on as above.

Bishop et al do not teach isolating a diseased cell from the tissue of a subject (claim 3), laser capture microdissection (claims 4-5,9) or a reference cell from the same subject (elected species of claim 17).

**Bonner et al** teach, throughout the document and especially column 19 second full paragraph, isolation of cellular material using laser capture microdissection. Bonner et al teach in table 1, isolation of normal and tumor tissue from the same patient (matched pairs).

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to analyze normal and tumor tissue from the same patient using laser capture microdissection per Bonner for susceptibility to the Ras Pathway inhibitors per Bishop et al.

One of ordinary skill in the art would have been motivated to use the analysis technique concerning normal and tumor tissue from the same patient using laser capture microdissection per Bonner for determining susceptibility to the Ras Pathway inhibitors per Bishop et al. because of the speed and efficiency afforded by laser capture microdissction, as noted by Bonner in column 19, line 60.

One of ordinary skill could use the analysis technique concerning normal and tumor tissue from the same patient using laser capture microdissection per Bonner for determining susceptibility to the Ras Pathway inhibitors per Bishop et al. with a reasonable expectation of success since Bonner et al provide many examples of using laser capture microdissection to generate samples for cancer prognosis and treatment (see columns 20-28).

Claims 1,2,7,14-15,20-23,36-39,41-42 and 26,27,29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Bishop et al** (US Patent 6,316,462) in view of **Bilodeau et al** (US Patent Applicaiton 2002/0137755) as evidenced by Tortora et al (Clinical Cancer Research 9:1566-1572).

**Bishop et al** is relied on as above.

Bishop et al do not teach a combination of targeting EGFR phosphorlyation along with targeting a non-voltage gated calcium ion channel blocker (elected two species from claim 26) or a specific Cox-2 inhibitor or carboxyamidotriazole (CAI) (elected two species from claims 30-31).

**Bilodeau et al** teach, throughout the document and especially the abstract and paragraph 0004, compounds that inhibit tyrosine kinases, and in particular, EGFR. Bilodeau et al teach the use of carboxyamidotriazole (CAI), which is a non-voltage gated calcium ion channel blocker, according to page 55 of the instant specification and set forth in claims 27 and 30.

Bilodeau et al teach in paragraph 0209, COX-2 inhibitors including celecoxib and rofecoxib, as set forth in claims 30 and 31.

Totorta et al teach on page 1567, third full paragraph that COX-2 is involved in the prostaglandin pathway, thus a COX-2 inhibitor represents a prostaglandin pathway effector, as set forth in claim 30.

Absent evidence to the contrary, targeting multiple different pathways (i.e. protaglandin, EGFR, non-voltage gated calcium channels) would prevent shunting around a single pathway, as set forth in claim 27.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to add the EGFR inhibitor(s) plus CAI or a COX-2 inhibitor(s) per Bilodeau et al to the Ras pathway inhibitor(s) assay of Bishop et al.

One of ordinary skill in the art would have been motivated to use the EGFR inhibitor(s) plus CAI or a COX-2 inhibitor per Bilodeau et al with Ras pathway inhibitor(s)

**Bonner et al** teach, throughout the document and especially table 1, multiple samples (repeated) comparing normal vs. tumor (diseased) cells.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention to add the EGFR inhibitor(s) plus CAI or a COX-2 inhibitor(s) to the Ras pathway inhibitor(s) assay of Bishop et al in view of Bilodeau et al and repeat the steps of claim 1 with multilple samples comparing normal vs. tumor cells per Bonner et al.

One of ordinary skill in the art would have been motivated to use the EGFR inhibitor(s) plus CAI or a COX-2 inhibitor(s) to the Ras pathway inhibitor(s) assay per Bishop et al in view of Bilodeau et al and repeat the steps of claim 1 with multilple samples comparing normal vs. tumor cells per Bonner et al in an effort to provide sufficient material for statistically meaningful analysis, as noted by Bonner et al in column 11, line 63.

Additionally, combining one therapeutic agent plus other(s), know in the art for treating cancer, such as set forth in claim 40 represents combining equivalents known for the same purpose (treating cancer, according to Moon et al) and as set forth In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980), it is prima facie obvious to combine two [or more] compositions, each of which is taught by the prior art, in order to form a third composition to be used for the very same purpose.

One of ordinary skill could use the EGFR inhibitor(s) plus CAI or a COX-2 inhibitor(s) to the Ras pathway inhibitor(s) assay per Bishop et al in view of Bilodeau et al and repeat the steps of claim 1 with multilple samples comparing normal vs. tumor

assay per Bishop et al because the tyrosine kinase inhibitors of Bilodeau et al are useful in combination with other anti-cancer agents, as noted by Bilodeau et al in paragraph 0193.

One of ordinary skill could use the EGFR inhibitor(s) plus CAI or a COX-2 inhibitor per Bilodeau et al with Ras pathway inhibitor(s) assay per Bishop et al with a reasonable expectation of success since Bilodeau provide thorough synthetic protocols and an activity assay (see paragraphs 314-518).

Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Bishop et al** (US Patent 6,316,462) **in view of Bilodeau et al** (US Patent Applicaiton 2002/0137755) as applied to claims 1,2,7,14-15,20-23,36-39,41-42 and 26,27,29-31 above, and further in view of **Bonner et al** (US Patent 6,251,516) as evidenced by Tortora et al (Clinical Cancer Research 9:1566-1572) and Moon et al (US Patent Application 2005/0282849)

**Bishop et al in view of Bilodeau et al** is relied on as above.

Totorta et al teach on page 1567, third full paragraph that COX-2 is involved in the prostaglandin pathway, thus a COX-2 inhibitor represents a prostaglandin pathway effector, as set forth in claim 30.

Moon et al teach in paragraph 0200, that COX-2 inhibitors, CAI and tyrosine kinase inhibitors are all useful agents in treating cancer.

Bishop et al in view of Bilodeau et al do not teach repeating the steps of claim 1 for a second diseased cell, as set forth in claim 40.

cells per Bonner et al with a reasonable expectation of success since Bonner et al provide many examples of using laser capture microdissection to generate samples for cancer prognosis and treatment (see columns 20-28).

Claims 1,2,7,14-15,20-23,36-39,41-42 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Bishop et al** (US Patent 6,316,462) in view of **Lubman et al** (US Patent Application 2005/0230315).

**Bishop et al** is relied on as above.

Bishop et al do not teach reverse phase protein microarray analysis (claim 11) or phosphoprotein specific antibodies (claim 12)

**Lubman et al** teach, throughout the document and especially paragraphs 0010 and 0012, analysis of protein microarrays using phosphorylation specific antibodies featuring in line reverse phase HPLC.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to analyze protein microarrays with phosphoprotein specific antibodies and in line reverse phase HPLC per Lubman et al to assess the activity of the Ras pathway inhibitor(s) of Bishop et al.

One of ordinary skill in the art would have been motivated to use protein microarrays analyzed with phosphoprotein specific antibodies and in line reverse phase HPLC per Lubman et al to assess the activity of the Ras pathway inhibitor(s) of Bishop et al because it would have provided an efficient automated system with better resolution, as noted by Lubman in paragraph 0007.

One of ordinary skill could use protein microarrays with phosphoprotein specific antibodies and in line reverse phase HPLC per Lubman et al to assess the activity of the Ras pathway inhibitor(s) of Bishop et al with a reasonable expectation of success since Lubman et al provide many examples concerning identification of phosphorylated proteins from cells (see paragraphs 0246-0319).

Claims 1,2,7,14-15,20-23,36-39,41-42and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Bishop et al** (US Patent 6,316,462) in view of **Jain et al** (2000 IEEE Transactions on Pattern Analysis and Machine Intelligence 22:4-37 – IDS entry 9/3/2004).

**Bishop et al** is relied on as above.

Bishop et al do not teach pattern recognition (claim 25)

**Jain et al** teach, throughout the document and especially the abstract and tables 1-2, pattern recognition as providing a means of machine aided classification of various data sets by various methods including template matching, statistical, syntactic, neural networks, etc.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to analyze the assays concerning the Ras pathway inhibitor(s) of Bishop et a utilizing pattern recognition per Jain et al.

One of ordinary skill in the art would have been motivated to use pattern recognition per Jain et al in analyzing the assays concerning the Ras pathway

inhibitor(s) of Bishop because pattern recognition is the best possible way of utilizing sensors (such as protein microarrays), as noted by Jain on page 4.

One of ordinary skill could use pattern recognition per Jain et al in analyzing the assays concerning the Ras pathway inhibitor(s) of Bishop with a reasonable expectation of success since pattern recognition is well established in the art, being studied for over 50 years, according to Jain et al in the abstract.

Claims 1,2,7,14-15,20-23,36-39,41-42 and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Bishop et al** (US Patent 6,316,462) in view of **Moller et al** (US Patent 6,626,044).

**Bishop et al** is relied on as above.

Bishop et al do not teach a decrease in the activity state (claim 43) or a decrease in phosphorlyation (claim 44)

**Moller et al** teach, throughout the document and especially the abstract and column 1, lines 50-61 compounds that inhibit protein tyrosine phosphatases, which dephosphorylate phosphoproteins to proteins.

Absent evidence to the contrary, the phosphatase inhibitors of Moller would lead to an *increase* in phosphoproteins, such as phosphorylated ERK because the action of the Ras pathway kinases would not be reversible *in vivo.*

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to use the phosphatase inhibitors of Moller et al in lieu of the Ras pathway Inhibitor(s) in the ERK assay of Bishop et al.

One of ordinary skill in the art would have been motivated to use the phosphatase inhibitors of Moller et al in lieu of the Ras pathway Inhibitor(s) in the ERK assay of Bishop et al because the phosphatase inhibitors of Moller et al are useful in the treatment of type I and II diabetes, proliferative diseases, such as cancer, etc. as noted by Moller in column 10, lines 46-56.

One of ordinary skill could use the phosphatase inhibitors of Moller et al in lieu of the Ras pathway Inhibitor(s) in the ERK assay of Bishop et al with a reasonable expectation of success since Moller et al provide thorough synthetic protocols and an activity assay (see columns 32-95).

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/189808 in view of **Bishop et al** (US Patent 6,316,462) and in further view of **Jain et al** (2000 IEEE Transactions on Pattern Analysis and Machine Intelligence 22:4-37 – IDS entry 9/3/2004)

Instant claim 25 is drawn to a method comprising (i) measuring the activity states for a plurality of signaling proteins extracted from a diseased cell; (ii) determining whether the activity state of the signaling proteins is different, as compared to a reference cell *using pattern recognition*; (iii) and selecting a combination of at least two therapeutic agents.

Reference claim 1 is drawn to a method of classifying a biological state by the detection of discriminatory patterns where the discriminatory pattern describes the biological state.

The reference claim lacks a combination of therapeutic agent, however Bishop et al teach a variety of therapeutic agents including the farnesyl transferase inhibitor SCH 66336 and additional Ras signaling pathway inhibitors (e.g. PD 98059 or U0126).

The instant claims lack a classification scheme, however Jain et al teach in figure 1, that the first step of pattern recognition involves classification.

One of ordinary skill in the art would have been motivated to use a combination therapeutic agents, such as those suggested by Bishop et al because the combination is less toxic and has dramatic antitumor activity as noted by Bishop in column 4 line 29-30.

One of ordinary skill in the art would have been further motivated to classify data for pattern recognition per Jain et al concerning therapeutic agents, such as those suggested by Bishop et al because pattern recognition is the best possible way of utilizing sensors (such as protein microarrays), as noted by Jain on page 4.

This is a provisional obviousness-type double patenting rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

MARK L. SHIBUYA
PRIMARY EXAMINER